Thomas Packard Follow
Scientist | PhD Immunology | Postdoc @ Gladstone Institutes | Innate Immunity & HIV | all opinions posted ...
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Think HIV is cured? Not yet.

HIV "Cures" Should Be Published Research, Not Clickbait.

A recent publication by the Sunday Times exclaimed "British scientists hopeful for HIV cure" (1). Subsequent retreads of this article resulted in headlines of "remarkable" and "may have been cured!" **Of course, touting a cure for HIV is much more likely to generate a click than publishing the gritty truth of research—I mean, I clicked on it.**

I'm a scientist currently working on HIV cure research at the Gladstone Institutes in San Francisco. Nothing excites me more than the possibility of a cure for this awful, deadly disease, which—to many people's surprise—infects more than 5,000 people every day around the world. The need for a cure is real, and the sooner the better. Could this finally be it?

Unfortunately, the study described in the article is far from declaring an HIV cure.

Lack of Detectable Virus Does Not Equal Cure

The most glaring limitation is that the single patient (only 1 out of a potential 50-patient trial) the article claims to have undetectable HIV *is on antiretroviral therapy*. Though this is great for the patient—he's being effectively treated—

it is common for individuals on antiretroviral regimens to have undetectable levels of virus in the blood. However, this does not mean the individual is cured. HIV can remain latent—or asleep—and undetectable in a cell for years, only to reactivate at a later time.

We in the HIV field define a "cure" as lack of detectable virus *in the absence of antiretroviral therapy*. To measure this, the patient must be given "time to rebound" following treatment. In practice, this means a patient is treated while on antiretroviral drugs, following which they are taken off all medications and monitored for the virus to return. HIV "rebound" takes about two weeks in a typical HIV patient after interruption of antiretroviral therapy, and in some cases rebound can be very delayed, but still returns (see Boston patients or Mississippi baby).

HIV rebound has not been measured in this patient, not to mention the other 49 individuals in the study, and a publication is not expected until 2018, so **declaring an HIV cure is premature. But is it also dangerous?**

When talking about my research, I'm frequently asked, "Isn't HIV cured? Why study it anymore?" This perception is a real problem, as it translates to a lack of willingness to support and fund HIV cure research.

The good news is that this misperception somewhat stems from the great successes of antiretroviral therapy. Many HIV-positive individuals can have complete remission and live a relatively normal life. However, the overlooked facets are that these people must stay on antiretroviral therapy for life (with potentially severe side effects), and we need to get these life-saving drugs to everyone infected with HIV around the world—over 35 million people, for the rest of their lives.

This is why I continue to work on cure research; because we need a real option for a cure or vaccine to effectively fight HIV. The problem is not solved, and it's dangerous and irresponsible to prematurely declare victory and cry "cure." Public perceptions are important in driving the political will to fund scientific research, and if the public thinks HIV is cured—or almost cured—research may suffer.

Shock & Kill

As for the approach in the British study, the good news is that it follows a well-accepted strategy we call "shock & kill." Though the Times described it as "the first therapy created to track down and destroy HIV in every part of the body —including in the dormant cells that evade current treatments," there are already completed, published early-stage clinical trials using drugs to reverse

latency in HIV-infected patients (2). The basic principle is that hidden, latent HIV is reactivated so that the immune system can find the infected cells and kill them.

One of the mechanisms that hides HIV is *epigenetic silencing*. The British trial, like others before it, uses a drug called an *HDAC inhibitor* to remove this epigenetic silencing in an attempt to reactivate the latent virus. However, removing inhibition is not the most effective "shock" approach. Instead, the best treatment may lie in the potentially synergistic approach of combining an HDAC inhibitor with a drug that directly activates HIV. Thus, the British clinical trial may only result in a fraction of the latent HIV being revealed, leaving a reservoir of the virus still hidden in the body.

Additionally, simply reactivating HIV isn't enough. As the HIV has integrated into the host cell, we must also kill the cell to remove the virus. The British trial uses a vaccine to address this problem, but it's too early to tell whether this strategy will work, as no current vaccines have been found to be broadly effective in humans.

The Need for Responsible Reporting

It's great that news organizations are excited about HIV cure research, I am too! However, we must think critically about the titles and content that describe research. Let's not get so carried away with the desire to draw clicks that public misperception is generated with eye-catching headlines. Increasing misperception of research is dangerous as it may lead to decreases in funding, both from government grants and private philanthropy, for critical research on a real cure for HIV.